```
* * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * * *

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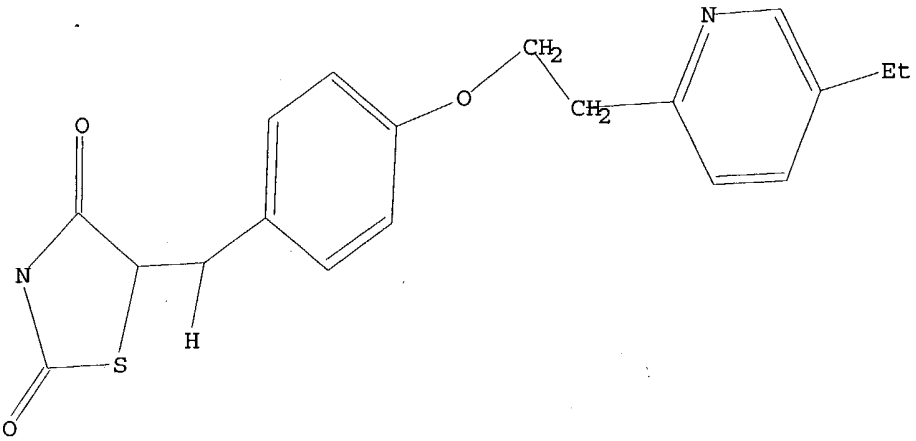


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Structure attributes must be viewed using STN Express query preparation.


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L3            13 SEA SSS FUL L1

=> file ca

=> s l3
L4           844 L3

=> s l3/prep
             844 L3
         3191721 PREP/RL
L5            25 L3/PREP
                 (L3 (L) PREP/RL)

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Uploading 1.str

L6      STRUCTURE UPLOADED

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L6 HAS NO ANSWERS
L6               STR
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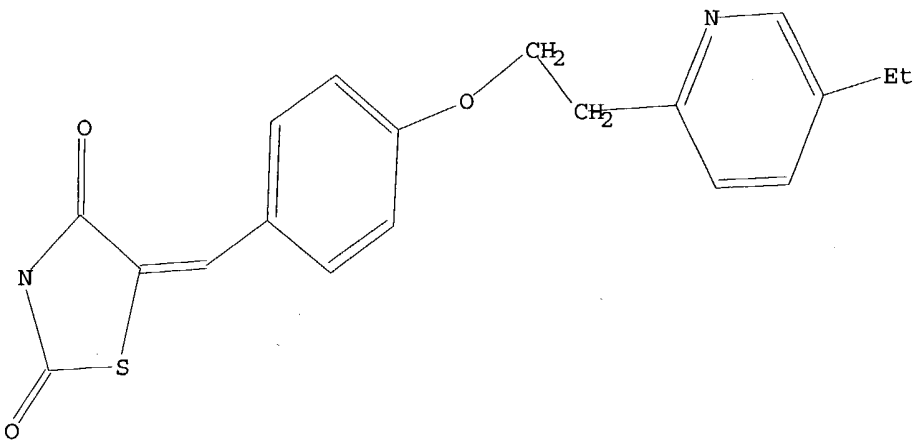

Structure attributes must be viewed using STN Express query preparation.

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L7             3 SEA SSS FUL L6

=> file ca

=> s l5 and l7
               12 L7
L8             10 L5 AND L7

=> d ibib abs hitstr 1-10
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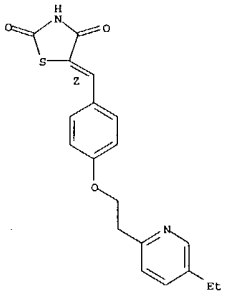
L8 ANSWER 1 OF 10 CA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 140:390934 CA
TITLE: Recoverable, Reusable, Highly Active, and Sulfur-Tolerant Polymer Incarcerated Palladium for Hydrogenation
AUTHOR(S): Okamoto, Kuniaki; Akiyama, Ryo; Kobayashi, Shu
CORPORATE SOURCE: Graduate School of Pharmaceutical Sciences, University of Tokyo, Tokyo, 113-0033, Japan
SOURCE: Journal of Organic Chemistry (2004), 69(8), 2871-2873
CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A new type of immobilized palladium, PI (polymer incarcerated) Pd, prepd. from Pd(PPh3)4 and the copolymer has been developed. The excellent activity of PI Pd has been demonstrated in hydrogenation of various olefins, benzyl ethers, and nitro and arom. compds. PI Pd is tolerant under high pressure and high temp. and can be recovered and reused several times without loss of activity even under harsh conditions. Moreover, PI Pd is highly resistant to poisoning by sulfur.

IT **136401-69-9**
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. and use of a recoverable, reusable, highly active, and sulfur-tolerant polymer incarcerated palladium catalyst for hydrogenation reactions)

RN 136401-69-9 CA
CN 2,4-Thiazolidinedione, 5-[[4-[2-(5-ethyl-2-pyridinyl)ethoxy]phenyl]methylene]-, (5Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

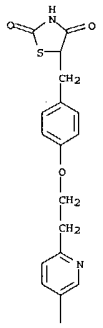


L8 ANSWER 1 OF 10 CA COPYRIGHT 2004 ACS on STN (Continued)

IT **111025-46-8P**, Pioglitazone
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(prepn. and use of a recoverable, reusable, highly active, and sulfur-tolerant polymer incarcerated palladium catalyst for hydrogenation reactions)

RN 111025-46-8 CA
CN 2,4-Thiazolidinedione, 5-[[4-[2-(5-ethyl-2-pyridinyl)ethoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

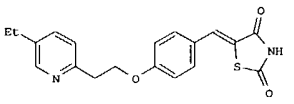


PAGE 2-A

Et

REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 10 CA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 140:217543 CA
TITLE: Optimization of the Reduction of a 5-Benzylidenethiazolidine-2,4-dione Derivative Supported by the Reaction Response Surface Analysis: Synthesis of Pioglitazone Hydrochloride
AUTHOR(S): Les, Andrzej; Pucko, Wieslaw; Szelejewski, Wieslaw
CORPORATE SOURCE: Pharmaceutical Research Institute, Warsaw, 01-793, Pol.
SOURCE: Organic Process Research & Development (2004), 8(2), 157-162
CODEN: OPRDFK; ISSN: 1083-6160
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

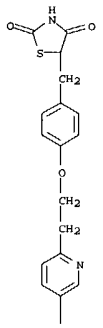
AB Significant improvements were made in the C:C bond redn. of the (benzylidene)thiazolidinedione I, an intermediate in the synthesis of pioglitazone hydrochloride. A reaction response surface anal. was applied to a series of expts. carried out under various conditions (temp., time, amt. of a catalyst and redn. reagents, purifn. of the substrate).

IT **111025-46-8P**, Pioglitazone **144809-28-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(optimization studies for the redn. of (benzylidene)thiazolidinedione deriv., the intermediate in the prepn. of pioglitazone hydrochloride, supported by the reaction response surface anal.)

RN 111025-46-8 CA
CN 2,4-Thiazolidinedione, 5-[[4-[2-(5-ethyl-2-pyridinyl)ethoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

L8 ANSWER 2 OF 10 CA COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



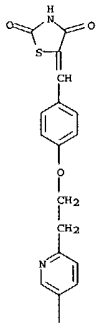
PAGE 2-A

Et

RN 144809-28-9 CA
CN 2,4-Thiazolidinedione, 5-[[4-[2-(5-ethyl-2-pyridinyl)ethoxy]phenyl]methylene]- (9CI) (CA INDEX NAME)

L8 ANSWER 2 OF 10 CA COPYRIGHT 2004 ACS on STN (Continued)

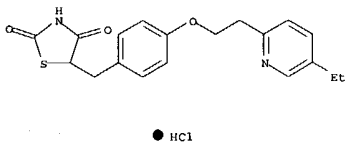
PAGE 1-A



PAGE 2-A

IT **112529-15-4P**, Pioglitazone hydrochloride
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(optimization studies for the redn. of (benzylidene)thiazolidinedione deriv., the intermediate in the prepn. of pioglitazone hydrochloride, supported by the reaction response surface anal.)
RN 112529-15-4 CA
CN 2,4-Thiazolidinedione,
5-[[4-[2-(5-ethyl-2-pyridinyl)ethoxy]phenyl]methyl]-, monohydrochloride (9CI) (CA INDEX NAME)

L8 ANSWER 2 OF 10 CA COPYRIGHT 2004 ACS on STN (Continued)



● HCl

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L8 ANSWER 3 OF 10 CA COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 140:111409 CA
TITLE: A novel process to prepare pioglitazone via several novel intermediates.
INVENTOR(S): Pandey, Bipin; Lohray, Vidya Bhushan; Lohray, Braj Bhushan
PATENT ASSIGNEE(S): Cadila Healthcare Limited, India
SOURCE: PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004007490	A2	20040122	WO 2003-IN241	20030715
WO 2004007490	A3	20040325		

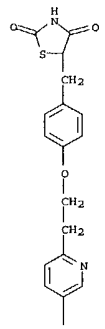
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: IN 2002-MU648 A 20020716

OTHER SOURCE(S): CASREACT 140:111409; MARPAT 140:111409
GI

L8 ANSWER 3 OF 10 CA COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A

RN 144809-28-9 CA
CN 2,4-Thiazolidinedione,
5-[[4-[2-(5-ethyl-2-pyridinyl)ethoxy]phenyl]methylene]- (9CI) (CA INDEX NAME)

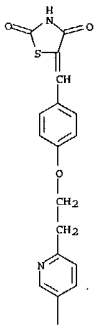
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention discloses a novel and general process to prep. various pyridine substituted 5-[4-[2-(alkyl substituted pyridyl)ethoxy]benzyl]-2,4-thiazolidinone derivs. of general formula I [R = alkyl], and their pharmaceutically acceptable salts. The present invention esp. provides a novel process to prep. pioglitazone hydrochloride [R = 5-ethyl], via novel intermediates, i.e. II and III. This process involves lesser no. of steps with high yields and uses key solid intermediates, which are operationally simple, and therefore offers opportunities for better com. viability.

IT **111025-46-8P 144809-28-9P**
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; RACT (Reactant or reagent); USES (Uses)
(prepn. of pioglitazone via several novel intermediates)
RN 111025-46-8 CA
CN 2,4-Thiazolidinedione,
5-[[4-[2-(5-ethyl-2-pyridinyl)ethoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

L8 ANSWER 3 OF 10 CA COPYRIGHT 2004 ACS on STN (Continued)

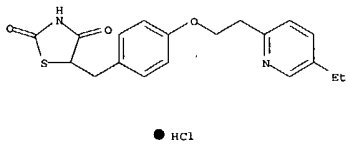
PAGE 1-A



PAGE 2-A

IT **112529-15-4P**
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(prepn. of pioglitazone via several novel intermediates)
RN 112529-15-4 CA
CN 2,4-Thiazolidinedione,
5-[[4-[2-(5-ethyl-2-pyridinyl)ethoxy]phenyl]methyl]-, monohydrochloride (9CI) (CA INDEX NAME)

L8 ANSWER 3 OF 10 CA COPYRIGHT 2004 ACS on STN (Continued)



● HCl

L8 ANSWER 4 OF 10 CA COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 140:59637 CA
TITLE: A process for the production of 5-[4-[2-(5-ethyl-2-pyridylethoxy)benzyl]-2,4-thiazolidinedione hydrochloride
INVENTOR(S): Adiyaman, Mustafa; Guner, Didem; Yurdakul, Aycil; Ridvanoglu, Nurten
PATENT ASSIGNEE(S): EOS Eczacibasi Ozgun Kimyasal Urunler Sanyi ve Ticaret A.S., Turk.
SOURCE: PCT Int. Appl., 15 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004000810	A1	20031231	WO 2002-TR25	20020619

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: WO 2002-TR25 20020619

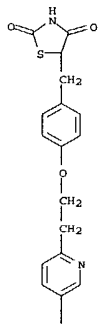
OTHER SOURCE(S): CASREACT 140:59637; MARPAT 140:59637

AB 5-[4-[2-(5-Ethyl-2-pyridylethoxy)benzyl]-2,4-thiazolidinedione hydrochloride is prepd. in high yield and selectivity by the esterification of 2-(5-ethyl-2-pyridyl)ethanol with methanesulfonyl chloride to give 2-(5-ethyl-2-pyridyl)ethyl methanesulfonate which is then etherified with 4-hydroxybenzaldehyde in the presence of KI to give 4-[2-(5-ethyl-2-pyridyl)ethoxy]benzaldehyde which is then subjected to an Aldol condensation with 2,4-thiazolidinedione in the presence of piperidine to give 5-[4-[2-(5-ethyl-2-pyridyl)ethoxy]benzylidene]-2,4-thiazolidinedione which is reduced with sodium borohydride to give 5-[4-[2-(5-ethyl-2-pyridyl)ethoxy]benzyl]-2,4-thiazolidinedione, which, upon salification with hydrogen chloride gives 5-[4-[2-(5-ethyl-2-pyridyl)ethoxy]benzyl]-2,4-thiazolidinedione hydrochloride.

IT **111025-46-8P 144809-28-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(in a process for the prodn. of 5-[4-[2-(5-ethyl-2-pyridylethoxy)benzyl]-2,4-thiazolidinedione hydrochloride)
RN 111025-46-8 CA
CN 2,4-Thiazolidinedione,
5-[[4-[2-(5-ethyl-2-pyridinyl)ethoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

L8 ANSWER 4 OF 10 CA COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A

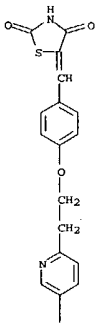


PAGE 2-A

RN 144809-28-9 CA
CN 2,4-Thiazolidinedione,
5-[[4-[2-(5-ethyl-2-pyridinyl)ethoxy]phenyl]methylene]- (9CI) (CA INDEX NAME)

L8 ANSWER 4 OF 10 CA COPYRIGHT 2004 ACS on STN (Continued)

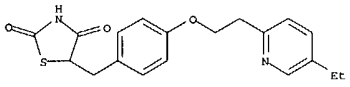
PAGE 1-A



PAGE 2-A

IT **112529-15-4P**
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(process for the prodn. of
5-[4-[2-(5-ethyl-2-pyridylethoxy)benzyl]-2,4-
thiazolidinedione hydrochloride)
RN 112529-15-4 CA
CN 2,4-Thiazolidinedione,
5-[[4-[2-(5-ethyl-2-pyridinyl)ethoxy]phenyl]methyl]-
, monohydrochloride (9CI) (CA INDEX NAME)

L8 ANSWER 4 OF 10 CA COPYRIGHT 2004 ACS on STN (Continued)



● HCl

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L8 ANSWER 5 OF 10 CA COPYRIGHT 2004 ACS on STN

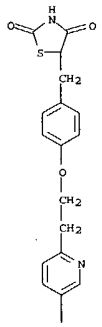
ACCESSION NUMBER: 139:86976 CA
TITLE: Catalytic hydrogenation of exocyclic double bonds in production of thiazolidinedione antihyperglycemics
INVENTOR(S): Dolitzky, Ben-zion
PATENT ASSIGNEE(S): Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals Usa, Inc.
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003053367	A2	20030703	WO 2002-US41278	20021220
WO 2003053367	A3	20030904		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 2003153765	A1	20030814	US 2002-324928	20021220
PRIORITY APPLN. INFO.:			US 2001-342437P P	20011220

OTHER SOURCE(S): CASREACT 139:86976
AB A method of catalytic hydrogenation of the exocyclic double bond of a penultimate thiazolidinedione precursor comprises (a) providing a soln. of the penultimate thiazolidinedione precursor in a high capacity solvent, (b) combining the soln. with a supported metal hydrogenation catalyst in a reactor, and (c) exposing the mixt. of the soln. and the hydrogenation catalyst to hydrogen gas. The method is used in prodn. of a thiazolidinedione antihyperglycemic drugs, such as pioglitazone, troglitazone, and rosiglitazone. Thus, 5-[[4-[2-(5-ethyl-2-pyridinyl)ethoxy]phenyl]methylene]-2,4-thiazolidinedione (50 g), DMF (250 mL) and Pd/C (50 g) were charged into an autoclave. The hydrogenation was carried out at 3 atm of H2 pressure at 50.degree. for 72 h to convert 68.5% of the starting material and afford pioglitazone contg. 3.5% of impurities.
IT **111025-46-8P**, Pioglitazone
RL: IMF (Industrial manufacture); **PREP (Preparation)**
(catalytic hydrogenation of exocyclic double bonds in prodn. of thiazolidinedione antihyperglycemics)
RN 111025-46-8 CA
CN 2,4-Thiazolidinedione,
5-[[4-[2-(5-ethyl-2-pyridinyl)ethoxy]phenyl]methyl]-
(9CI) (CA INDEX NAME)

L8 ANSWER 5 OF 10 CA COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A

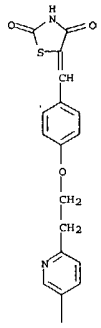


PAGE 2-A

IT **144809-28-9**
RL: RCT (Reactant); RACT (Reactant or reagent)
(catalytic hydrogenation of exocyclic double bonds in prodn. of thiazolidinedione antihyperglycemics)
RN 144809-28-9 CA
CN 2,4-Thiazolidinedione,
5-[[4-[2-(5-ethyl-2-pyridinyl)ethoxy]phenyl]methyle
ne]- (9CI) (CA INDEX NAME)

L8 ANSWER 5 OF 10 CA COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A

L8 ANSWER 6 OF 10 CA COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 137:169513 CA

TITLE: Method for preparing compounds derived from thiazolidinedione, oxazolidinedione or hydantoin

INVENTOR(S): Bulliard, Michel; Derrien, Yvon; Pintus, Tony

PATENT ASSIGNEE(S): Ppg-Sipsy, Fr.

SOURCE: PCT Int. Appl., 15 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: French

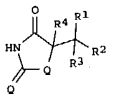
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002064577	A2	20020822	WO 2002-FR571	20020214
WO 2002064577	A3	20030103		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
FR 2820741	A1	20020816	FR 2001-2010	20010214
FR 2820742	A1	20020816	FR 2001-5206	20010417
EP 1360179	A2	20031112	EP 2002-704834	20020214
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2002006967	A	20040309	BR 2002-6967	20020214
JP 2004520401	T2	20040708	JP 2002-564510	20020214
US 2004059121	A1	20040325	US 2003-636155	20030807
PRIORITY APPLN. INFO.:			FR 2001-2010 A	20010214
			FR 2001-5206 A	20010417
			WO 2002-FR571 W	20020214

OTHER SOURCE(S): CASREACT 137:169513; MARPAT 137:169513

GI



I

AB Title compds. I [Q, Q1 = O, S; R1, R2 = H, alkyl, cycloalkyl, alkylaryl,

L8 ANSWER 6 OF 10 CA COPYRIGHT 2004 ACS on STN (Continued)

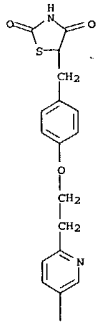
arylalkyl, optionally substituted by alkyl, alkoxy, aryloxy, halogen, hydroxy, sulfino, sulfonyl, amino; R3, R4 = H] were prepd. by reducing I [R3R4 = bond] with HCO2H in presence of a transition metal catalyst, and optionally a cosolvent. Thus, I [Q = S, Q1 = O, R1 = H, R2 = 4-[2-(5-ethyl-2-pyridyl)ethoxy]phenyl (Q2), R3R4 = bond] was treated with HCO2H and H in presence of Pd-C at 75-80.degree. for 6 h to give 97.4% pioglitazone [I, Q = S, Q1 = O, R1 = R3 = R4 = H, R2 = Q2].

IT **111025-46-8P**, Pioglitazone
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); **PREP (Preparation)**
(prepn. of thiazolidinediones, oxazolidinediones or hydantoin by redn. of their alkylidene derivs.)

RN 111025-46-8 CA

CN 2,4-Thiazolidinedione, 5-[[4-[2-(5-ethyl-2-pyridinyl)ethoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

IT **144809-28-9**
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of thiazolidinediones, oxazolidinediones or hydantoin by redn. of their alkylidene derivs.)

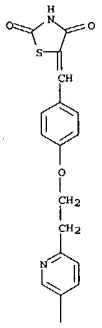
RN 144809-28-9 CA

CN 2,4-Thiazolidinedione, [illegible]ethyl-2-pyridinyl)ethoxy]phenyl]methyle

L8 ANSWER 6 OF 10 CA COPYRIGHT 2004 ACS on STN (Continued)

nel- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

L8 ANSWER 7 OF 10 CA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 128:127942 CA
TITLE: Process for preparing 4-(2-(2-pyridyl)ethoxy)benzaldehyde derivatives
INVENTOR(S): Saito, Yuzuru; Mizufune, Hideya; Yamashita, Makoto
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan
SOURCE: Eur. Pat. Appl., 15 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 816340	A1	19980107	EP 1997-304554	19970626
EP 816340	B1	20030423		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 5952509	A	19990914	US 1997-880638	19970623
CA 2208878	AA	19971227	CA 1997-2208878	19970626
CA 2208878	C	20020820		
JP 10072438	A2	19980317	JP 1997-170637	19970626
JP 3256841	B2	20020218		
AT 238282	E	20030515	AT 1997-304554	19970626
PT 816340	T	20030829	PT 1997-304554	19970626
ES 2191811	T3	20030916	ES 1997-304554	19970626
US 6100403	A	20000808	US 1999-292384	19990412
PRIORITY APPLN. INFO.:			JP 1996-167862 A	19960627
			US 1997-880638 A3	19970623

OTHER SOURCE(S): MARPAT 128:127942
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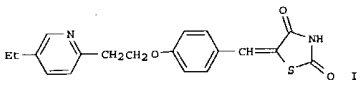
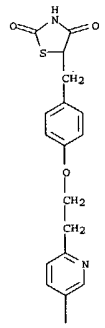


I

AB 4-(2-(2-Pyridyl)ethoxy)benzaldehydes, which are useful as starting compds. for producing thiazolidinedione derivs. with hypoglycemic and hypolipidemic activities, are prepd. by treating a 2-(2-pyridyl)ethyl sulfonate with 4-HOC6H4CHO in a lower alc. in the presence of an alkali metal or alk. earth metal carbonate. Thus, 2-(5-ethyl-2-pyridyl)ethanol was converted to its mesylate and treated with 4-HOC6H4CHO and K2CO3 in EtOH-PhMe for 5 h at 80.degree. to give 78.9% 4-(2-(5-ethyl-2-pyridyl)ethoxy)benzaldehyde. This compd. was treated with 2,4-thiazolidinedione to give the benzylidenethiazolidinedione I in 61.4% overall yield from 2-(5-ethyl-2-pyridyl)ethanol.

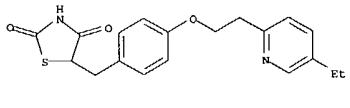
L8 ANSWER 7 OF 10 CA COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A

IT **112529-15-4P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(prepn. of 4-(2-(2-pyridyl)ethoxy)benzaldehyde derivs.)
RN 112529-15-4 CA
CN 2,4-Thiazolidinedione, 5-[[4-[2-(5-ethyl-2-pyridinyl)ethoxy]phenyl]methyl]-, monohydrochloride (9CI) (CA INDEX NAME)

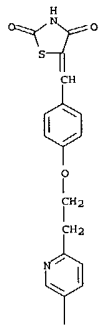


● HCl

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS

L8 ANSWER 7 OF 10 CA COPYRIGHT 2004 ACS on STN (Continued)
IT **144809-28-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of 4-(2-(2-pyridyl)ethoxy)benzaldehyde derivs.)
RN 144809-28-9 CA
CN 2,4-Thiazolidinedione, 5-[[4-[2-(5-ethyl-2-pyridinyl)ethoxy]phenyl]methylene]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

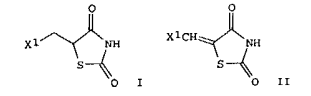
IT **111025-46-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; RACT (Reactant or reagent); USES (Uses)
(prepn. of 4-(2-(2-pyridyl)ethoxy)benzaldehyde derivs.)
RN 111025-46-8 CA
CN 2,4-Thiazolidinedione, 5-[[4-[2-(5-ethyl-2-pyridinyl)ethoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

L8 ANSWER 7 OF 10 CA COPYRIGHT 2004 ACS on STN (Continued)
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

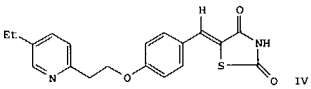
L8 ANSWER 8 OF 10 CA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 119:249944 CA
TITLE: Regioselective reduction of substituted 5-(methylene)thiazolidinediones
INVENTOR(S): Huber, Joel Edward
PATENT ASSIGNEE(S): Upjohn Co., USA
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9313095	A1	19930708	WO 1992-US10329	19921204
W: AU, BB, BG, BR, CA, CS, FI, HU, JP, KP, KR, LK, MG, MN, MW, NO, NZ, PL, RO, RU, SD, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG				
AU 9332310	A1	19930728	AU 1993-32310	19921204
EP 618915	A1	19941012	EP 1993-900732	19921204
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 07502530	T2	19950316	JP 1992-511663	19921204
JP 2766730	B2	19980618		
CA 2122712	C	19990921	CA 1992-2122712	19921204
US 5585495	A	19961217	US 1994-397130	19940617
PRIORITY APPLN. INFO.:			US 1991-811103	A2 19911220
			WO 1992-US10329	A 19921204

OTHER SOURCE(S): CASREACT 119:249944; MARPAT 119:249944
GI

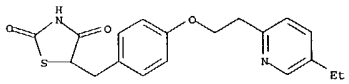

I

II


IV

AB The title process comprises producing compds. I (X1 = org. residue), by

IT **112529-15-4P**, Pioglitazone hydrochloride
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(prepn. of, by regioselective redn.)
RN 112529-15-4 CA
CN 2,4-Thiazolidinedione,
5-[[4-[2-(5-ethyl-2-pyridinyl)ethoxy]phenyl]methyl]-, monohydrochloride (9CI) (CA INDEX NAME)

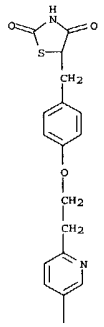


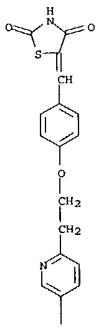
● HCl

IT **144809-28-9**
RL: RCT (Reactant); RACT (Reactant or reagent)
(regioselective redn. of)
RN 144809-28-9 CA
CN 2,4-Thiazolidinedione,
5-[[4-[2-(5-ethyl-2-pyridinyl)ethoxy]phenyl]methylene]- (9CI) (CA INDEX NAME)

regioselectively reducing compds. II with a Co ion, a ligand (e.g., dimethylglyoxime, 2,2'-bipyridyl, 1,10-phenanthroline), and a reducing agent (e.g., NaBH4, LiBH4, KBH4, etc.). This process is conducted at -20.degree. to +45.degree. and over comes many of the problems of prior-art redn. processes which required troublesome high-pressure hydrogenations using Pd/C catalysts, and is esp. suited for the prepn. of Pioglitazone hydrochloride (III). Thus, thiazolidinedione IV was slurried in water and 50% aq. NaOH soln., dimethylglyoxime, powd. blue indicating silica gel (contg. .apprx.0.7% CoCl2) added, NaBH4 added, and DMF added. The intermediate III free base was reacted with HCl in AcOEt, producing III.

IT **111025-46-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(prepn. and reaction of, with hydrochloric acid)
RN 111025-46-8 CA
CN 2,4-Thiazolidinedione,
5-[[4-[2-(5-ethyl-2-pyridinyl)ethoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)





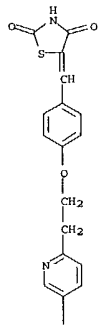
L8 ANSWER 9 OF 10 CA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 118:6971 CA
TITLE: Preparation of ether-containing 2,4-thiazolinedione derivatives
INVENTOR(S): Arita, Miichiro; Mizuno, Yukio
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan
SOURCE: Eur. Pat. Appl., 7 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 506273	A2	19920930	EP 1992-302233	19920316
EP 506273	A3	19930113		
EP 506273	B1	19950531		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, PT, SE				
CA 2063851	AA	19920926	CA 1992-2063851	19920324
CA 2063851	C	20030624		
JP 05112483	A2	19930507	JP 1992-66368	19920324
US 5554758	A	19960910	US 1995-474133	19950607
PRIORITY APPLN. INFO.:			JP 1991-60208 A	19910325
			US 1992-855798 B1	19920323
			US 1993-121291 B1	19930915
			US 1994-352184 B1	19941201

OTHER SOURCE(S): MARPAT 118:6971
AB Title compds. ACH2CH2OB (A = aryl, R1CO, R2CH:CH, wherein R1, R2 = aliph. hydrocarbyl, arom. hydrocarbyl, heterocyclyl, arylalkyl, alicyclyl; B = aryl) useful as intermediates for, among others, medicines, are prepd. by reacting ACH2CH2X (X = leaving group) with MOB (M = alkali metal, alk. earth metal) in a nonaq. solvent. 2-(5-Ethyl-2-pyridyl)ethyl methanesulfonate (prepn. given) and 4-(OCH)C6H4OK were refluxed to give 4-[2-(5-ethyl-2-pyridyl)ethoxy]benzaldehyde. This was condensed with 2,4-thiazolidinedione to give the benzylidine deriv., which was hydrogenated to give 5-[4-[2-(5-ethyl-2-pyridyl)ethoxy]benzyl]-2,4-thiazolidinedione, which is active against diabetes (no data).
IT **144809-28-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and hydrogenation of)
RN 144809-28-9 CA
CN 2,4-Thiazolidinedione,
5-[[4-[2-(5-ethyl-2-pyridinyl)ethoxy]phenyl]methyle
ne]- (9CI) (CA INDEX NAME)

L8 ANSWER 9 OF 10 CA COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



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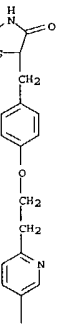

IT **111025-46-8P**
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(prepn. of, as antidiabetic)
RN 111025-46-8 CA
CN 2,4-Thiazolidinedione,
5-[[4-[2-(5-ethyl-2-pyridinyl)ethoxy]phenyl]methyl]-
(9CI) (CA INDEX NAME)

L8 ANSWER 9 OF 10 CA COPYRIGHT 2004 ACS on STN (Continued)

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PAGE 2-A

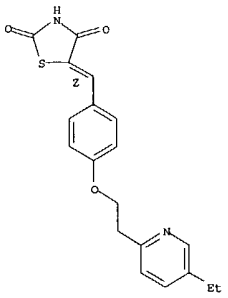
L8 ANSWER 10 OF 10 CA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 115:159025 CA
TITLE: Studies on antidiabetic agents. X. Synthesis and biological activities of pioglitazone and related compounds
AUTHOR(S): Momose, Yu; Meguro, Kanji; Ikeda, Hitoshi; Hatanaka, Chitoshi; Oi, Satoru; Sohda, Takashi
CORPORATE SOURCE: Res. Dev. Div., Takeda Chem. Ind., Ltd., Osaka, 532, Japan
SOURCE: Chemical & Pharmaceutical Bulletin (1991), 39(6), 1440-5
CODEN: CPBTAL; ISSN: 0009-2363
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The prepn. of pioglitazone (I) analogs II (R = H, 3-, 5-, 6-Me, 5-Et; R1 = H, Me; X = CH, N) and III (n = 1, 2; X1 = S, NH; Y = O, S; Y = O, S; Z = NH, NCH2CO2H, S) from phenyl- and pyridylethanols IV and the investigation of their structure activity relationships as antidiabetic and hypolipemic agents are reported. III (X1 = S; Y = O; Z = NH) were equipotent to I, however, other compds. were less active than I. Catalytic hydrogenation of III (R = 5-Et; R1 = H; n = 2; X = S; Y = O; Z = NH) was found to be a convenient route to I.
IT **136401-69-9P 136401-70-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and hypoglycemic and hypolipemic activity of)
RN 136401-69-9 CA
CN 2,4-Thiazolidinedione,
5-[[4-[2-(5-ethyl-2-pyridinyl)ethoxy]phenyl]methyle
ne]-, (5Z)- (9CI) (CA INDEX NAME)

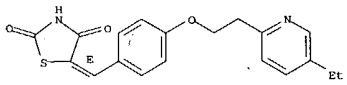
Double bond geometry as shown.

L8 ANSWER 10 OF 10 CA COPYRIGHT 2004 ACS on STN (Continued)



RN 136401-70-2 CA
CN 2,4-Thiazolidinedione,
5-[[4-[2-(5-ethyl-2-pyridinyl)ethoxy]phenyl]methylene]-, (E)- (9CI) (CA INDEX NAME)

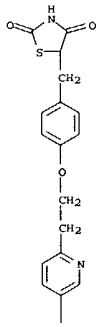
Double bond geometry as shown.



IT **111025-46-8P**, Pioglitazone
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(prepn. and hypoglycemic and hypolipidemic activity of)
RN 111025-46-8 CA
CN 2,4-Thiazolidinedione,
5-[[4-[2-(5-ethyl-2-pyridinyl)ethoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

L8 ANSWER 10 OF 10 CA COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A

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L2              0 S L1 SAM
L3             13 S L1 FULL

     FILE 'CA' ENTERED AT 10:37:57 ON 15 SEP 2004
L4            844 S L3
L5             25 S L3/PREP

     FILE 'REGISTRY' ENTERED AT 10:38:39 ON 15 SEP 2004
L6                STRUCTURE UPLOADED
L7              3 S L6 FULL

     FILE 'CA' ENTERED AT 10:39:01 ON 15 SEP 2004
L8             10 S L5 AND L7

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---Logging off of STN---


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Executing the logoff script...


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STN INTERNATIONAL LOGOFF AT 10:39:59 ON 15 SEP 2004
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